THE METABOLISM OF GLYCOLIC ACID

BY

SAM SILBERGELD

B. S., University of Chicago, 1939
M.S., University of Illinois, 1941

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN
CHEMISTRY IN THE GRADUATE SCHOOL OF
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INTRODUCTION

Although there is little definitely known about the metabolism of glycolic acid, it has been suggested that glycolic acid is involved in the metabolism of glycine and arginine, of glycols, of glyoxal, of glycolaldehyde, and of certain organic acids, especially glyoxylic, citric, acetoacetic, and oxalic. Most of these suggested relationships, however, rest on scanty or inconclusive evidence.

In the last two years glycolic acid has become commercially available at a sufficiently low cost to be used in foodstuffs. However, before this is done, it is essential to determine whether glycolic acid ingestion may prove injurious.

The purpose of the present investigation was to study the metabolism of glycolic acid in order to determine the nature of the substances resulting from its oxidation in the animal body and to detect toxic effects, if any, produced by its ingestion or injection.

EXPERIMENTAL

The metabolism of glycolic acid was studied by the following methods:

A. The Oxidation of Glycolic Acid by Tissue Slices.

Tissue slice studies were carried out in Warburg flasks almost exactly as described by Warburg[1] and Faigen[2]. In addition, an experiment was carried out in which 0.01 mg. of glycolic acid was added to each Warburg flask, and tests for glycolic (as well as glyoxylic) acid were made by means of 2,7-dihydroxynaphthalene after two hours shaking with liver slices.

The results showed that liver slices can oxidize glycolic acid to an end product other than glyoxylic acid.

B. The Effects of Glycolic Acid in Prolonged Rat Feeding Experiments.

Albino rats were used in these experiments. The various diets used consisted of a commercial rat food and various levels of glycolic acid (0.5, 1.0, and 2.0 per cent) or sodium glycolate (1.0 per cent). The experiments lasted for 218-248 days during which time the growth rate, the excretion of glycolic (as well as glyoxylic) acid and toxic effects were noted.

The results clearly indicate that the growth of rats is decreased by the addition of one or two per cent of glycolic acid to the diet, while one-half per cent has little or no effect. Furthermore, as shown by 2,7-dihydroxynaphthalene tests, the excretion of glycolic acid by rats always occurs on a two per cent glycolic acid diet, often occurs on a one per cent diet, and rarely occurs on a one-half per cent diet. This indicates that rats have the ability to catabolize at least 0.05-0.08 gm. of glycolic acid to a product other than glyoxylic acid.

Several rats on the one and two per cent glycolic acid diets died during the course of the experiment. Examination of these animals revealed gross kidney pathology. The kidneys were therefore removed and preserved in fixing fluids. At the termination of the experiment, kidneys were removed from additional animals. Histological examination of these kidneys revealed that many of the pathological ones contained masses of crystalline material. In order to determine the nature of the crystals, sections of the kidneys were analyzed for oxalic acid by the procedure of Dodds and Gallimore[3].

It was found that glycolic acid when fed to male rats on a one per cent or two per cent level of the diet results in an increase in the oxalate content of the kidneys, and as shown by gross and histological examination, most of the kidneys from the male rats on the one per cent level are abnormal, whereas, all of the kidneys from the male rats on the two per cent level are abnormal. In contrast, glycolic acid fed to female rats on

a one or two per cent level does not result in an increased oxalate content of the kidneys, and gross and histological examination of the kidneys show them to be normal.

C. The Acute Effects of Glycolic Acid in the Rabbit.

The acute effects of sodium glycolate on kidney function were investigated following a procedure similar to that used by Rose[4] in studying the nephrotoxic effects of dicarboxylic acids. Of the rabbits used in the present experiments, one served as a control, two received by subcutaneous injections 0.5 grams of glycolic acid as the sodium salt, and two received in the same manner 1.0 grams of glycolic acid as the sodium salt. The rabbits drank water, **ad libitum,** but received no food during the experimental period of seven days in order to avoid the possible influence of food consumption upon blood composition and upon the toxic effects in question. In each experiment blood non-protein nitrogen and creatinine levels were determined both before and after injection of sodium glycolate. Renal function was tested by means of the phenolsulfonphthalein test.

The results indicate that the injection into rabbits of 0.5-1.0 gm. of glycolic acid as its sodium salt causes no immediate renal damage.

D. The Chronic Effects of Glycolic Acid in the Rabbit.

Of the five rabbits used, one male and one female served as controls and were given daily, **ad libitum,** a stock diet of a commercial rabbit food. Of the other three rabbits, all received the stock diet, and in addition, received in their drinking water either 0.25 or 0.50 gm. of sodium glycolate, or 0.5 gm. of glycolic acid per kilogram of body weight per day for about seven months. Phenolsulfonphthalein tests and blood non-protein nitrogen determinations showed no indications of nephrotoxic effects. Oxalate analyses at the termination of the experiment indicated that glycolic acid had caused a definite increase in the oxalate content of the kidneys.

SUMMARY

Small amounts of glycolic acid can be oxidized by the animal body to an end product other than glyoxylic acid. The growth of rats is decreased by the presence of glycolic acid at a level of one or two per cent of the diet. When administered over a long period of time to rabbits, glycolic acid caused an increase in kidney oxalate; however, when fed to rats, only the males on a one and two per cent glycolic acid level showed an increase in kidney oxalate and gave evidence of toxic effects.

Thus the present investigation furnishes evidence that glycolic acid, like glycol and glyoxylic acid, is oxidized to oxalic acid in the animal body and thereby exerts a toxic effect.

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VITA

The author was born March 1, 1918, at Wengrov, Poland. He came to this country in 1923 and became an American citizen January 29, 1926. He was reared at Carlinville, Illinois, where he obtained his elementary and high school education and attended Blackburn College from 1936-1938. During 1938-1939, he attended the University of Chicago and received the Bachelor of Science degree in December, 1939. In September, 1940, he began graduate study at the University of Illinois where he held a Special Research Assistantship in Biochemistry during 1941-1942, and a Teaching Assistantship in Inorganic Chemistry from September, 1942-October, 1943.

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